A=Milliliters of perchloric acid reagent used in titrating the samples;
B=Milliliters of perchloric acid reagent used in titrating the blank;
m=Percent moisture content of the sample.

Calculate the difference between the potency and the ampicillin content as follows:

Difference=(Potency in micrograms per milligram/10)−percent ampicillin content.

(6) *Crystallinity.* Proceed as directed in §436.203(a) of this chapter.

(7) *Identity.* Proceed as directed in §436.211 of this chapter, using an 0.5 percent potassium bromide disc, prepared as described in paragraph (b)(1) of that section.

[39 FR 18976, May 30, 1974, as amended at 46 FR 16683, Mar. 13, 1981; 49 FR 3458, Jan. 27, 1984; 50 FR 19918, May 13, 1985]

§440.7a Sterile ampicillin trihydrate.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Ampicillin trihydrate is the trihydrate form of D(-)α-aminobenzyl penicillin. It is so purified and dried that:

(i) It contains not less than 900 micrograms and not more than 1,050 micrograms of ampicillin per milligram on an anhydrous basis.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its loss on drying is not less than 12 percent and not more than 15 percent.

(vi) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 3.5 and not more than 6.0.

(vii) Its ampicillin content is not less than 90 percent on an anhydrous basis.

(viii) The acid-base titration concordance is such that the difference between the percent ampicillin content when determined by nonaqueous acid titration and by nonaqueous base titration is not more than 6. The potency-acid titration concordance is such that the difference between the potency value divided by 10 and the percent ampicillin content of the sample determined by the nonaqueous acid titration is not more than 6. The potency-base titration concordance is such that the difference between the potency value divided by 10 and the percent ampicillin content of the sample determined by the nonaqueous base titration is not more than 6.

(ix) It is crystalline.

(x) It gives a positive identity test for ampicillin trihydrate.

(2) *Labeling.* In addition to the labeling requirements prescribed by §432.5(b) of this chapter, this drug shall be labeled ''ampicillin.''

(3) *Requests for certification; samples.* In addition to complying with the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, loss on drying, pH, ampicillin content, concordance, crystallinity, and identity.

(ii) Samples required:

(*a*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(*b*) For sterility testing: 20 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use any of the following methods; however, the results obtained from the microbiological agar diffusion assay shall be conclusive:

(i) *Microbiological agar diffusion assay.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Dissolve an accurately weighed portion of the sample in sufficient sterile distilled water to give a stock solution containing 0.1 milligram of ampicillin per milliliter. Further dilute an aliquot of the stock solution with 0.1*M* potassium phosphate buffer, pH 8.0 (solution 3) to the reference concentration of 0.1 microgram of ampicillin per milliliter (estimated).

(ii) *Iodometric assay.* Proceed as directed in §436.204 of this chapter, except in paragraph (d) of that section, add 3 drops of 1.2*N* hydrochloric acid to both the sample and working standard solutions after the addition of 0.01*N* iodine solution.

(iii) *Hydroxylamine colorimetric assay.* Proceed as directed in §436.205 of this chapter.

(2) *Sterility.* Proceed as directed in §436.20 of this chapter, using the method described in paragraph (e)(1) of that section, except in lieu of paragraph (e)(1)(i)(*a*), prepare the sample for test as follows: From each of 10 immediate

containers, aseptically transfer approximately 300 milligrams of sample into a sterile 500-milliliter Erlenmeyer flask containing approximately 400 milliliters of diluting fluid D. Add at least 200,000 Levy units[1] of penicillinase. Repeat the process using 10 additional containers. Swirl both of the stoppered flasks to completely solubilize the suspension prior to filtration and proceed as directed in paragraph (e)(1)(ii) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(f) of this chapter, using a solution containing 20 milligrams of ampicillin per milliliter.

(4) [Reserved]

(5) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(7) *Ampicillin content.* Proceed as directed in § 436.213 of this chapter, using both the titration procedures described in paragraph (e)(1) and (2) of that section. Calculate the ampicillin content as follows:

(i) *Acid titration.*

Percent ampicillin content=[(A − B) (normality of lithium methoxide reagent) (349.4) (100) (100)]/[(Weight of sample in milligrams) (100 − *m*)].

where:

A=Milliliters of lithium methoxide reagent used in titrating the sample;

B=Milliliters of lithium methoxide reagent used in titrating the blank;

m=Percent moisture content of the sample.

Calculate the difference between the potency and the ampicillin content as follows:

Difference=(Potency in micrograms per milligram/10) − percent ampicillin content.

(ii) *Base titration.*

Percent ampicillin content=[(A − B) (normality of perchloric acid reagent) (349.4) (100) (100)]/[(Weight of sample in milligrams) (100 − *m*)].

where:

A=Milliliters of perchloric acid reagent used in titrating the samples;

B=Milliliters of perchloric acid reagent used in titrating the blank;

m=Percent moisture content of the sample.

Calculate the difference between the potency and the ampicillin content as follows:

Difference=(Potency in micrograms per milligram/10) − percent ampicillin content.

(8) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

(9) *Identity.* Proceed as directed in § 436.211 of this chapter, using a 0.5 percent potassium bromide disc, prepared as described in paragraph (b)(1) of that section.

[39 FR 18976, May 30, 1974, as amended at 46 FR 16683, Mar. 13, 1981; 49 FR 3458, Jan. 27, 1984; 50 FR 19918, May 13, 1985]

§ 440.8 Bacampicillin hydrochloride.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Bacampicillin hydrochloride is the hydrochloride salt of the 1–ethoxycarbonyloxyethyl ester of ampicillin. It is a white powder. It is so purified and dried that:

(i) Its potency is not less than 623 micrograms and not more than 727 micrograms of ampicillin per milligram on an ''as is'' basis.

(ii) [Reserved]

(iii) Its moisture content is not more than 1.0 percent.

(iv) Its pH in an aqueous solution containing 20 milligrams per milliliter is not less than 3.0 and not more than 4.5.

(v) It passes the identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, and identity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(i) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii) of this chapter, except:

[1] One Levy unit of penicillinase inactivates 59.3 units of penicillin G in 1 hour at 25° C. and at a pH of 7.0 in a phosphate buffered solution of a pure alkali salt of penicillin G when the substrate is in sufficient concentration to maintain a zero order reaction.